**Interim Report**
**OPTN/UNOS HISTOCOMPATABILITY COMMITTEE**

**Teleconference**
**May 14, 2007**
**1:00-3:00 (EST)**

- M. Sue Leffell, Ph.D., Committee chair, opened the meeting by introducing Takashi Maki, M.D., Ph.D, from Beth Israel Deaconess Medical Center; he will be replacing Lisa Cuchara, Ph.D. as the Region 1 representative to the Committee. She also introduced Helen (Hongfei) Li, M.D., M.P.H., and Ph.D., who will be the representative from the Health Resources and Services Administration (HRSA).

- Membership Issues and Report from the Membership and Professional Standards Committee (MPSC). The full Committee approved the recommendations regarding key personnel changes in UNOS-approved HLA laboratories made by the Committee's Membership subcommittee on a conference call held April 10, 2007, Geof Land, Ph.D. had presented these recommendations to the MPSC on May 1, 2007. (Committee Vote: 15 for, 0 against, 1 abstention)

  Dr. Land also reported that the MPSC reviewed a tremendous number of evaluations of problem centers and programs. Chief among the violations being examined were ABO violations, and noncompliance due to specimen mislabeling. Dr. Land said the MPSC showed zero tolerance for both. He also mentioned that the living donor group, of which he is a member, has joined with several other representatives from various committees to develop a joint living donor proposal.

  Dr. Baxter-Lowe commented that she had a problem with specimen mislabeling at her center. She sent such complaints directly to her OPO, but nothing came of it. Several other Committee members echoed her experience. Dr. Land requested that in the future Committee members send such reports to the MPSC.

- Implementation of Policy 3.5.11.3 Calculated Panel Reactive Antibody (CPRA). The Board approved the Histocompatibility Committee's proposed modifications to policy 3.5.11.3 at its December 2006 meeting. As a result, calculated PRA (CPRA) will replace PRA when determining kidney allocation.

  The Histocompatibility Committee recommended that implementation happen in three phases:

  - Phase One, allocation continues to be based on traditional PRA. OPOs, transplant centers, and HLA laboratories will be able to calculate and see CPRA on match runs. The CPRA calculator will become available to members at this time.

  - Phase Two, allocation will be based on CPRA. OPOs, transplants centers, and HLA laboratories will be able to enter and see traditional PRA on the waitlist if desired.

  - Phase Three, allocation is based on CPRA. Traditional PRA information will no longer appear on the waitlist.

  Dielita McKnight, from the UNOS IT Department, reported programming for Policy 3.5.11.3 (CPRA) was on schedule. Phase One is scheduled to be implemented September 2007.

Ms. McKnight asked Committee members what timeframe the Committee envisions between Phase One and Phase Two. The Committee decided that a specific timeframe should not be set at this time. The Committee plans to monitor the reaction of the transplant community and examine the results of the implementation of Phase One before moving on to Phase Two.

Ann Harper, from the UNOS Research Department, noted two remaining issues with the calculation of CPRA. She reminded the Committee that HLA equivalences used in the match are contained in Appendix 3A – HLA A, B and DR Antigen Values and Split Equivalences Table of UNOS policy. Not all equivalences currently needed for the CPRA calculation are contained in this table. For example, the equivalences for Bw4, Bw6, Dr51, DR52, and DR53 are not listed. Ms. Harper suggested that an additional table of equivalences be included in the Appendix that would list these equivalences, to be use in the CPRA calculation only.

Ms. Harper also reported that a few alleles do not have population frequencies. If a center were to list such an allele as a candidate's single unacceptable antigen, the corresponding CPRA value would be zero. She said this was a rare occurrence with only about 20 instances found in 20,000 candidates; however, she was concerned that if there were a candidate on the cusp of receiving sensitivity points, it could make a difference in the allocation. Jerry Rosenberg, M.D., Ph.D. asked about the origin of the frequencies being used for the calculation of CPRA. Dr. Leffell answered that they came from OPTN data and were published in the April 15, 2007 issue of *Transplantation*, volume 83:964-972.

A subcommittee was formed to review these issues and report to the full Committee in July. Lea Ann Baxter-Lowe, Ph.D, Diane Pidwell, Ph.D. and Dr. Leffell volunteered to serve on this subcommittee.

- Letters to the Kidney and Pancreas Transplantation Committees. At a previous Histocompatibility Committee meeting, Alan Leichtman, M.D., the Scientific Registry of Transplant Recipients (SRTR) representative, suggested that the Committee write formal letters to the Kidney Committee making specific recommendations for the new kidney allocation system. Dr. Leffell offered to write two letters; Dr. Baxter-Lowe wrote a third.

    - Virtual Crossmatch and Allocation for Sensitized Candidates

        Dr. Leffell thought that this letter was necessary because of a concern within the Histocompatibility Committee that members of the transplant community were using the term "virtual cross match" in conjunction with the CPRA policy. The Histocompatibility Committee opines it is vital to clarify that the immediate goals of the CPRA policy are to provide improved prediction of crossmatch outcome, as opposed to a "virtual crossmatch."

        Dr. Leichtman said it is important that this letter be sent to the Kidney Committee because it is considering giving highly sensitized candidates a higher priority based on their CPRA value. He said it is wise to clarify to the Kidney Committee the limitations of CPRA.

        The committee reviewed and approved the letter with some minor suggestions.

    - Inclusion of HLA matching in a "LYFT"- based kidney allocation system. (The term "life years from transplant," or LYFT, is now being used to describe the net benefit concept.)

        The Histocompatibility Committee has reviewed information from the Kidney Public Forum held February 8, 2007 and data from the Scientific Registry of Transplant Recipients (SRTR) on the LYFT simulations and the contribution of covariates to the LYFT score. The Committee became aware of a proposed simulation removing the contribution of HLA-A and B matching to LYFT to

determine if this change would increase allocation to minority candidates. Because the Histocompatibility Committee will not have an opportunity to review and comment on the data from these simulations before the Kidney Transplant Committee considers possible revisions to renal allocation, they are raising a concern. The Histocompatibility Committee recommends that the appropriate weight in the LYFT scores should be given for the degree of HLA match and that the Kidney Transplantation Committee consider these data carefully before any further consideration of removal of HLA-A and B from the LYFT calculations.

The Committee reviewed and approved the letter with some minor changes.

- 0MM for Pediatric Candidates

  The Committee is concerned that the simulations from the SRTR using LYFT underestimate the advantage of HLA matching for pediatric patients and young adults. Dr. Leichtman assured the Committee that kidney allocation for pediatric candidates would not change under the new kidney allocation scheme currently being discussed by the Kidney Committee, thus preserving the 0MM priority for pediatric candidates.

  Even so, the Committee asked to see a simulation that would provide 0MM priority to pediatric candidates. Dr. Baxter-Lowe volunteered to work with Dr. Leichtman in drafting this request and will present it to the full Committee in July.

The Committee decided not to send a letter to the Kidney Committee concerning inclusion of 0MM for pediatric candidates at this time. It may reconsider upon receipt of the simulation requested.

- Implementation of CPRA for Candidates Undergoing Desensitization. Following the approval of replacing panel reactive antibody (PRA) with a calculated PRA, the OPTN/UNOS Histocompatibility Committee has received comments concerning the potential impact of this policy on sensitized transplant candidates who are undergoing "desensitization" while waiting for a deceased donor transplant. Representatives of Transplant Centers that offer these desensitization protocols have raised the concern that the requirement to list sufficient unacceptable antigens to achieve a CPRA of 80 or greater to be eligible for the extra "PRA points" may adversely impact their candidates. If a candidate is successfully desensitized to certain HLA antigens, these should no longer be listed as unacceptable, but if these antigens are not listed, then that candidate may no longer be eligible for the advantage afforded to other sensitized patients via the PRA points. It is argued that the success of these desensitization programs relies on the ability to lower a candidate's antibody levels sufficiently to obtain crossmatch compatibility within a "window of opportunity" before antibody levels rebound. Because the benefit of PRA points will facilitate their transplantation, it has been requested that some exception be made for candidates whose antibody levels have been successfully diminished.

  Several members of the committee said that this situation could be handled by an alternative system. Under this system, highly sensitized candidates with CPRA of 80 or greater who undergo and receive successful reduction of circulating HLA specific antibodies would be permitted to retain eligibility for the four PRA points without listing sufficient unacceptable antigens to obtain a CPRA of 80 or greater. Such candidates will be awarded this eligibility provided that the HLA antigens to which they retain specific antibodies are listed as unacceptable. Eligibility for PRA points without listing of unacceptable antigens will only be permitted for a finite period. This time period should be determined by the Kidney Transplant Committee upon receipt of data regarding the length of time that antibody levels remain suppressed following successful desensitization.

These data should be provided by Centers requesting this exception.

The Committee approved sending a letter about a possible alternative system for desensitization to the Kidney Committee to be reviewed at its next meeting.

- Request for Incorporating CPRA into an Existing Alternative System for Kidneys.

The OPTN/UNOS Board approved the following resolution in November 2006:

> ** RESOLVED, that the modifications to Policy 3.5.11.3 (Panel Reactive Antibody) approved by the Board of Directors shall pertain to all OPOs operating with approved alternative systems for assigning priority in sensitized kidney candidates as well as the national kidney allocation system, unless application is made by an OPO to incorporate the use of a Calculated PRA (CPRA) into its existing alternative system. Such applications must be made in accordance with Policy 3.4.7.1 and be presented to the Histocompatibility Committee no later than February 1, 2007. OPOs may maintain the components of alternative systems that are not affected by the Histocompatibility Committee's implementation of CPRA as set forth in Policy 3.5.11.3

An OPO that would like to continue its alternative system for the allotment of sensitization points could make a formal request to continue its alternative system incorporating CPRA. If the OPO does not make this request, its alternative system for assigning priority in sensitized candidates would convert to the national system described in Policy 3.5.11.3.

The Tennessee Transplant Society (TTS), which uses a statewide sharing agreement for the allocation of kidneys, made a formal request to the OPTN/UNOS Histocompatibility Committee to incorporate CPRA into its alternative system. Currently, Tennessee gives four points to kidney transplant candidates with a PRA of 80 percent or higher, as is done in the national allocation system. TTS also assigns 2 points to candidates with a PRA of 40-79 percent.

Representing the TTS, Deborah Crowe, Ph.D., presented data to the Histocompatibility Committee on a conference call held on February 22, 2007. She used OPTN data from the last 12 months to compare kidney allocation in Tennessee with the rest of the nation (Figures 1 and 2 below).

Based on these data, TTS requested to maintain the two extra points for candidates with a CPRA of 40-79 percent.

After reviewing the data, the Histocompatibility Committee unanimously voted to approve Tennessee's request. The Kidney Transplantation Committee also approved Tennessee's request by a unanimous vote at its May 20, 2007 meeting.

The following proposal will go out for public comment June, 2007 and be presented to the OPTN/UNOS Board of Directors in September 2007.

*Request for Incorporating CPRA into an Existing Alternative System for Kidneys*

Sensitized kidney waiting list candidates within the state of Tennessee with defined unacceptable HLA antigens that yield an 80 percent or greater probability of incompatibility with deceased donors (CPRA) would be assigned four points; and those candidates that have a CPRA value between 40 percent-79 percent will be assigned two points. This is of interest to the Histocompatibility and Kidney Committees because a gradation of points for PRA > 20 percent is being considered as part of the new kidney allocation proposal. The Histocompatibility Committee noted that this request is in the spirit intended for variances, because it is designed to test a specific research question for a specified period of time, as shown below.

The proposed alternative system is expected to be in place for a maximum of three years or until the OPTN/UNOS Kidney Transplantation Committee implements the new Kidney Allocation System, which is currently under development. The Histocompatibility and Kidney Committees will then analyze the alternative system and will make a request to the Board of Directors to continue, modify, or terminate the system.

Dr. Steven Geier, Ph.D. suggested the numbers of candidates available in Tennessee may not be large enough to justify giving priority to the moderately sensitized candidate. He suggested that the SRTR model this request. Dr. Leichtman asked that the Committee put together a formal request to present to the SRTR at the next meeting. Dr. Land volunteered to help write the request.

- Resolved and Unresolved Discrepant Typings Report. Lori Gore, Committee Liaison, reported to the Committee that this report is currently not working as intended. Ms. Gore asked the Committee for direction regarding the report, and a review of the original intent of and current need for the report. A subcommittee including Ann Harper, Diane Kumashiro, M.S., CHS, and Jerry Rosenberg, M.D., Ph.D., will report back to the Committee in July.

- Programming change that would require HLA for an electronic kidney offer. Ms. Gore reported that with the implementation of DonorNet®, OPOs can run kidney, kidney/pancreas, and pancreas matches without donor HLA.This is a violation of policy 3.5.9.1 (Essential Information for Kidney Offers). Several transplant programs have complained about offers being made without donor HLA. During the February, 22, 2007 conference call, the Histocompatibility Committee approved a programming change that would close match runs made without HLA at zero.

  Ms. Gore reported that LifeGift Organ Donation Center objected when the implementation notice for this change was circulated, citing a local variance.

  The UNOS IT staff was able to reach a compromise with LifeGift that would not delay programming. The OPO may continue its practice until CPRA goes into effect, after which it must comply with the requirement to enter donor HLA. January 2008 is the anticipated implementation date for CPRA.

- New Business, Dr. Leffell introduced several new topics for Committee consideration and later discussion.

  First, she asked the Committee to consider developing a formal policy that would require transplant centers to share the data from candidates that have been transferred from one center to another. This information would include previous transplant HLA and previous PRA. The problem that the Committee wished to address is that some laboratories do not maintain data or will not share it. Dr. Land mentioned that institutions are confused about HIPAA regulations and patient confidentiality. The Committee agreed that there was a need for a formal policy proposal. She also asked that Committee members consider the following questions submitted by Dr. Geier:

  1. Should UNOS expand the entry of patient current and historic PRA to class I and II PRA?

     - This could help to flag transplant programs that are not listing unacceptables for candidates with significant PRAs. It could also allow a comparison between PRA vs. CPRA.

  2. Should CPRA data be entered separately as class I and II unacceptables and CPRA, which would then be combined to produce a total CPRA?

     - This would allow analysis of the contribution of class I and II CPRAs to crossmatch results and ethnic and regional transplant outcomes.

**Members Present**

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| Susie Leffell, Ph.D. | Chair |
| J. Michael Cecka, Ph.D. | Vice Chair |
| Takashi Maki, M.D.Ph.D. | Region 1 |
| Dod Stewart, BS, CHS | Region 3 |
| Afzal Nikaein, Ph.D. | Region 4 |
| Lee Ann Baxter-Lowe, Ph.D. | Region 5 |
| Diane I Kumashiro,MS,CHS | Region 6 |
| Thomas W Sell, CHS, CLS | Region 7 |
| Steve Geier, Ph.D., | Region 8 |
| Charlene Hubbell, MT | Region 9 |
| Diane Pidwell, Ph.D. | Region 11 |
| Ron Kochik, B.S.N., RN | At Large |
| Deborah Miller, MPH, MT | At Large |
| Jerry Rosenberg, M.D., Ph.D., | At Large |
| Geof Land, Ph.D. | Ex Officio |
| Helen (Hongfei) Li, M.D Ph.D. M.P.H | Ex Officio (HRSA) |

**UNOS Staff**

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| Lori Gore | Committee Liaison |
| Wida Cherikh, Ph.D. | Data Liaison |
| Ann Harper | Data Liaison |
| Dielita McKnight | IT Liaison |

**SRTR**

Alan Leichtman, M.D.